REMARKS

Claims 1, 7-9, 18, 20 and 22 have been amended. Claims 16-17 have been cancelled. Claims 1-15 and 18-22 remain for consideration. No new matter has been added.

2. Claims 1-22 currently stand rejected under 35 U.S.C. §112, first paragraph for allegedly failing to comply with the written description requirement.

CLAIMS 1-15 AND 18-22

Applicants respectfully submit that these rejections are now moot since independent claims 1, 18 and 22 have been amended. See at least pages 29-30 of the amended application submitted on February 19, 2008 ("Amended Application") for support thereof.

CLAIMS 16-17

The Action contends that all pending claims – including claims 16-17 – are "*indefinite because the examiner is not sure what exactly a 'biological cell metabolizing excitation source' and/or a 'chemical cell metabolizing excitation source' are and additionally the above phrases/limitations were not described in the specification.*" (Action, pg 3-4). Applicants respectfully disagree. Specifically, neither claim 16 nor claim 17 recite the features of "*a biological cell metabolizing excitation source*" or "*a chemical cell metabolizing excitation source*". (see cl. 16 and 17). As a result, it is respectfully submitted that claims 16 and 17 comply with §112 and these rejections should be withdrawn.

3. Claims 1, 2 and 4-10 currently stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over U.S. Patent No. 6,469,785 to Duveneck et al. (hereinafter "Duveneck") in view of U.S. Patent No. 4,621,059 to Rokugawa (hereinafter "Rokugawa").

CLAIM 1

The Official Action acknowledges that "*Duveneck fails to disclose an excitation source connected to the inlet opening of the device.*" (Official Action, pg. 6). However, the Official Action then contends that Rokugawa teaches an excitation source and that it would have been obvious to one of ordinary skill in the art to have modified the device in Duveneck with the excitation source in Rokugawa. (Official Action, pg 6). This rejection is improper for several reasons.

A PRIMA FACIE CASE OF OBVIOUSNESS HAS NOT BEEN ESTABLISHED

The only support the Official Action cites for combining Duveneck and Rokugawa is because *"it was known in the art at the time to do so"*. (Official Action, pg. 6). However, as known, such circular reasoning is incapable of establishing a prima facie case of obviousness. Specifically, the Official Action is lacking the necessary technically thoughtful rational regarding why a skilled person would have combined the prior art references at the time of the invention. Accordingly, it is respectfully submitted that a prima facie case of obviousness has not been established.

IF COMBINED, DUVENECK NO LONGER WORKS FOR HIS INTENDED PURPOSE

If Duveneck is modified based upon the teachings of Rokugawa as suggested in the Official Action, then Duveneck would no longer be operable for its intended purpose.

Specifically, the Official Action contends that a skilled person would modify the system of Duveneck to include a source that provides a biological or chemical excitation medium via the inlet 64 of Duveneck. However, Duveneck teaches the use of an optical excitation source. Modifying Duveneck to receive a biological or chemical excitation medium from a reservoir source would change the entire detection principle of Duveneck, which relies upon the semiconductor laser 10 to radiate excitation light.

Duveneck teaches, as illustrated in FIG. 1, that "*[leading] into the measuring chamber 68 are an inlet channel 64 and an outlet channel 66 through which the fluid samples to be examined can be circulated through the measuring chamber 68 and past the sensor layer 8.*" (Duveneck, col. 7, lines 5-8). With regards to the measurement of analytes within the fluid sample, Duveneck teaches the following:

> "*The measuring method of the device... relies on the interaction of the evanescent light intensity with the sensor layer 8. The actual measurement can be carried out by radiating in the excitation light continuously, in continuous-wave (cw) operation, that is to say preferably with excitation at a light intensity that is constant with time. Alternatively, however, the measurement can be carried out by radiating in the excitation light in the form of timed pulses... with which the luminescence can be detected in a time-resolved manner....*" (col. 7, lines 56-67).

Thus, according to a fair and proper reading of Duveneck, optical excitation of the luminescent radiation occurs via the evanescent field within the waveguide 6. (Duveneck, col. 7, line 5-14 and 56-67). The luminescent radiation is NOT excited chemically or biologically, but instead optically by excitation radiation 70 created by a semiconductor laser 10 and coupled into an optical waveguide 6.

In contrast to Duveneck, Rokugawa teaches the following about an apparatus for measuring velocity of enzyme reaction:

> "*According to the present invention, there is provided an apparatus for measuring the velocity of an enzyme reaction wherein chemical substances react in the presence of catalyst of an enzyme. The apparatus comprises a capillary column in which the enzyme is immobilized, and solution supplying means for pumping a solution containing a chemical substance and a luminescent substance in the capillary column. When the solution flows through the column, the enzyme reaction is proceeded by the catalytic action of the enzyme and the reaction product and the luminescent substance react to emit light. Detecting means detects the luminescence in the capillary column to output a signal relative to the distribution of a luminescent intensity along the longitudinal direction of the column. A calculation unit inputting an output signal of the detecting means calculates the enzyme activity or the quantity of the chemical substance from the distribution of the luminescent intensity along the longitudinal direction of the capillary column by an end assay and/or a rate assay.*" (Rokugawa, col. 2, lines 14-34 and col. 5-6, emphasis added).

Thus, according to a fair and proper reading Rokugawa, the detected luminescence is created from the reaction between the chemical substances and the catalyst of the enzyme to be measured. (Rokugawa, col. 2, lines 14-34 and col. 5-6).

A person of ordinary skill in the art would NOT have been motivated to modify the device in Duveneck with the vessels 2, 12 in Rokugawa. Specifically, Duveneck teaches exciting the sample to be measured (the analyte) using an evanescent field via the semiconductor laser 10, whereas Rokugawa teaches exciting the sample to be measured (the enzyme) via a reaction between the chemical substances and catalyst of the sample. There would be no reasonable expectation of success by using both light sources (i.e., the substrate laser 10 of Duveneck and the chemical reaction of Rokugawa), since it would add an additional complex variable that would have to be accounted for by the light detector. For example, the light detector may not be able to distinguish between light emitted from and the intensity of the substrate laser 10 versus light emitted from the chemical reaction, and therefore could not properly measure sample characteristics. As a result, applicants respectfully submit that a person

of ordinary skill in the art would NOT have been motivated to modify the device of Duveneck with the vessels of Rokugawa.

CLAIMS 2 AND 4-10

Applicants respectfully submit that these rejections are moot since claim 1 is patentable for at least the reasons as set forth above.

4. Claim 3 currently stands rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Duveneck in view of Rokugawa and U.S. Patent No 6,104,495 to Sieben et al. (hereinafter "Sieben").

Applicants respectfully submit that this rejection is moot since claim 1 is patentable for at least the reasons as set forth above.

5. Claims 12 and 14 currently stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Duveneck in view of Rokugawa and PCT Application No. WO 2001/043875 to Schurmann-Mader et al. (hereinafter "Mader").

Applicants respectfully submit that these rejections are moot since claim 1 is patentable for at least the reasons as set forth above.

6. Claims 11 and 15 currently stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Duveneck in view of Rokugawa and U.S. Patent No. 5,278,048 to Parce et al. (hereinafter "Parce").

Applicants respectfully submit that these rejections are moot since claim 1 is patentable for at least the reasons as set forth above.

7. Claim 13 currently stands rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Duveneck in view of Rokugawa, Mader and U.S. Patent No. 5,582,697 to Ikeda et al. (hereinafter "Ikeda").

Applicants respectfully submit that this rejection is moot since claim 1 is patentable for at least the reasons as set forth above.

8. Claim 16 currently stands rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Mader in view of U.S. Patent No. 4,385,113 to Chapelle et al. (hereinafter "Chapelle").

Claim 16 has been cancelled.

9. Claims 18, 19 and 22 currently stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Duveneck in view Sieben.

CLAIM 18

As amended, claim 18 recites a device for detecting a cellular metabolic process associated with a cell by detecting a luminescence event in, at, or in the immediate vicinity of the cell. The device includes the features of:

> "*a semiconductive device with a surface prepared for coupling of the cell thereto;*
>
> *a detector for providing a luminescence signal indicative of the luminescent event, where the detector is integrated into the semiconductive device below the cell;*
>
> *a cover that covers the prepared surface to form a cavity, the cover having an inlet and an outlet; and*
>
> *a metabolically-influencing cell* ***excitation reservoir*** *fluidly coupled to the excitation medium inlet and configured to provide to the cavity via the inlet a*

> *biological or chemical excitation medium that includes a luminophore, where the excitation medium influences the metabolism of the cell during excitation thereof by the medium, and where the luminophore reacts with a metabolic product of the cell during the excitation thereof to provide luminescence detected by the detector.*" (cl. 18, emphasis added).

The Official Action contends that Duveneck teach the feature of "*an excitation source that provides to the cavity via the inlet a biological or chemical excitation medium that includes a luminophore.*" (Official Action, pg 15). The Official Action acknowledges that Duveneck "*fails to disclose that the device comprises a semiconductor device with the surface prepared for coupling the cell thereto.*" (Action, pg 15). However, the Official Action then contends that Sieben teaches a device for detecting signals related attached to a semiconductor body and that it would have been obvious to one of ordinary skill in the art to have modified the device in Duveneck with the semiconductor body in Sieben. (Official Action, pg 15). This rejection is improper for several reasons.

SIEBEN TEACHES AWAY FROM THE DEVICE IN DUVENECK

Duveneck teaches, as illustrated in FIG. 1, that "*[at] a position opposite the surface-emitting semiconductor laser, the waveguide 6 has a coupling-in grating 60 which bends radiation 70 emitted by the surface-emitting semiconductor laser in order to couple it into the waveguide 6 so that, in a preferred manner, only one or few modes 72 propagate in the waveguide. The light propagating in the waveguide preferably has a divergence of less than 5°.*" (Duveneck, col. 7, lines 33-39). Thus, according to a fair and proper reading of Duveneck, the coupling-in grating 60 is required to bend the radiation 70 emitted from the semiconductor laser 10 such that only one or a few modes 72 propagate into the waveguide 6.

In contrast to Duveneck, Sieben teaches that "*[the] prior-art arrangements are disadvantageous in that the living cells are observed through an optical microscope, so that the measuring apparatus is open at one end or must have at least one optical window. This requires a relatively complex and costly measuring structure which is made in part of transparent material, particularly glass or optical plastic.*" (Sieben, col. 1, lines 13-19). Thus, according to a fair and proper reading, Sieben explicitly teaches away from using an optical window, such as the coupling-in grating 60 as taught in Duveneck due to cost and complexity. As a result, applicants respectfully submit that a person of ordinary skill in the art would not have been motivated to modify the device of Duveneck with the teachings of Sieben.

DUVENECK AND SIEBEN DO NOT TEACH THE FEATURES RECITED IN CLAIM 18

First, applicants respectfully submit that the Official Action has already acknowledged that "*Duveneck **fails** to disclose an excitation source connected to the inlet opening of the device.*" (Official Action, pg 6, lines 3-4, emphasis added). The Official Action makes this statement in the context of discussing claim 1, but of course what Duveneck teaches does not depend on the claims the present application.

Second, Duveneck teaches, as illustrated in FIG. 1, that "*[in] a housing 2, a photoelectric detection unit 4... and a surface-emitting semiconductor laser 10 serving as a light source are mounted on a carrier 76 which may be a component part of the housing.*" (Duveneck, col. 6, lines 48-52). "*Leading into the measuring chamber 68* [within the housing 2] *are an inlet channel 64 and an outlet channel 66 through which the fluid samples to be examined can be circulated through the measuring chamber 68 and past the sensor layer 8.*" (Duveneck, col. 7,

lines 5-8). With regards to the measurement of analytes within the fluid samples, Duveneck teaches the following:

> "*The measuring method of the device... relies on the interaction of the evanescent light intensity with the sensor layer 8. The actual measurement can be carried out by radiating in the excitation light continuously, in continuous-wave (cw) operation, that is to say preferably with excitation at a light intensity that is constant with time. Alternatively, however, the measurement can be carried out by radiating in the excitation light in the form of timed pulses... with which the luminescence can be detected in a time-resolved manner....*" (Duveneck, col. 7, lines 56-67).

Thus, according to a fair and proper reading of Duveneck, the inlet channel 64 is merely used to circulate the fluid samples into the measuring chamber 68. (Duveneck, col. 7, lines 5-8 and 56-67). Specifically, Duveneck teaches radiating **excitation** light from a semiconductor laser 10 through fluid samples and detecting the radiated light to analyze the samples. That is, the light emitted from the laser 10, and NOT the fluid samples, induces the optical excitation.

Although the fluid samples may include luminophores (col. 19, lines 25-40), Duveneck does not teach or suggest that the fluid samples include any excitation medium. Significantly, the Amended Application teaches that "*[substances] exhibiting luminescence are known as luminophores.*" (pg 20). "*The excitation medium is chosen for example such that it influences the metabolism of the cell 6, so that metabolic processes become visible because of the luminophores referred to above and are detected by the detectors 2.*" (Amended Application, pg 30). That is, the present application explicitly distinguished between luminophores and an excitation medium – e.g., the excitation medium influences the metabolism of the cells such that the luminophores may show the metabolic process. (Amended Application, pg 20 and 30). Therefore, the feature of "*a metabolically-influencing cell **excitation** reservoir ...*" CANNOT be read on the inlet channel 64. As a result, assuming for the moment, without admitting, that the

device in Duveneck was modified with the teachings of Sieben, the combination still would not teach the feature of "*a metabolically-influencing cell excitation reservoir fluidly coupled to the excitation medium inlet...*" since, at most, the combination would merely teach optically exciting the analytes in the fluid samples using the semiconductor laser 10 as taught in Duveneck.

CLAIM 19

Applicants respectfully submit that this rejection is moot since claim 18 is patentable for at least the reasons as set forth above.

CLAIM 22

Applicants respectfully submit that claim 22 is patentable for at least similar reasons as set forth above with respect to claim 18.

10. Claim 20 currently stands rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Duveneck in view Sieben and Rokugawa.

Applicants respectfully submit that this rejection is moot since claim 18 is patentable for at least the reasons as set forth above. In addition, as set forth with respect to claim 1, Duveneck and Rokugawa are not properly combinable.

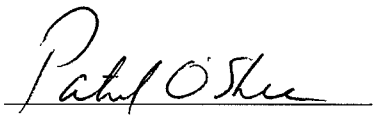
11. Claim 21 currently stands rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Duveneck in view Sieben and Mader.

Applicants respectfully submit that this rejection is moot since claim 18 is patentable for at least the reasons as set forth above.

For all the foregoing reasons, reconsideration and allowance of claims 1-15 and 18-22 is respectfully requested.

If a telephone interview could assist in the prosecution of this application, please call the undersigned attorney.

Respectfully submitted,



Patrick J. O'Shea
Reg. No. 35,305
O'Shea Getz P.C.
1500 Main Street, Suite 912
Springfield, MA 01115
(413) 731-3100, Ext. 102